Cont 19

(B) binding said adapter molecule to at least a portion of said adapter binding region created in step (A) to form a nucleic acid molecule:adapter molecule complex;

(C) optionally, ligating said target nucleic acid molecule to said adapter molecule such that at least said magnifying tag(s) remain associated with said target nucleic acid molecule;

(D) treating the resulting complex of step (B) or step (C) so that at least another region of said target nucleic acid molecule is converted into a form suitable for binding another adapter molecule, wherein said another region comprises one or more bases which are not associated with the magnifying tags of step (B); and thereafter

(E) repeating steps (B) to (D), with the proviso that the adapter molecule in each cycle of steps (B) to (C) binds to a region adjacent to a region of said target nucleic acid molecule to which the adapter molecule of a previous cycle bound, or the adapter molecule in each cycle of steps (B) to (C) binds to a region which overlaps with a region of said target nucleic acid molecule to which the adapter molecule of a previous cycle bound, and wherein the magnifying tags of each cycle of steps (A) to (C) are ligated together,

to thereby magnify said signal.

Claim 27. The method as claimed in Claim 26, wherein in step (A), said form is a single-stranded nucleic acid molecule.

Claim 28. The method as claimed in Claim 26, wherein said magnifying tag(s) correspond to one or more bases of said adapter binding region.

Claim 29. The method as claimed in Claim 26, wherein each magnifying tag corresponds to at least 2 bases in said adapter binding region or to at least 2 bases adjacent to said adapter binding region.

Claim 30. The method as claimed in Claim 26, wherein said magnifying tags together correspond to at least 2 bases in said adapter binding region or to at least 2 bases adjacent to said adapter binding region.

Claim 31. The method as claimed in Claim 30, wherein said magnifying tags together correspond to at least 4 bases in said adapter binding region or to at least 4 bases adjacent to said adapter binding region.

Claim 32. The method as claimed in Claim 26, wherein a chain of magnifying tags are associated with said target nucleic acid molecule.

Claim 33. The method as claimed in Claim 32, wherein said chain comprises 4 or more magnifying tags corresponding to at least 4 contiguous bases.

Claim 34. The method as claimed in Claim 26, wherein said magnifying tags are nucleic acid sequences of at least 2 bases in length.

Cont A 19

Claim 35. The method as claimed in Claim 34, wherein said magnifying tags are nucleic acid sequences of 10 to 30 bases in length.

Claim 36. The method as claimed in Claim 26, wherein said adapter molecule comprises a recognition site for a nuclease, which has a cleavage site separate from its recognition site.

Claim 37. The method as claimed in Claim 26, wherein said adapter molecule comprises recognition sites for 2 or more nucleases, which have cleavage sites separate from their respective recognition sites, wherein cleavage with said nucleases produces single-stranded regions which are adjacent or overlapping.

Claim 38. The method as claimed in Claim 26, wherein two or more adapter molecules are bound in step (B).

Claim 39. The method as claimed in Claim 38, wherein said adapter molecules are bound to overlapping or adjacent regions.

Claim 40. The method as claimed in Claim 39, wherein said adapter molecules are bound to overlapping regions thereby allowing the association of more than one magnifying tag with each base.

Claim 41. The method as claimed in Claim 26, wherein step (C) is performed.

Claim 42. The method as claimed in Claim 26, further comprising the step of:

(F) sequencing the target nucleic acid molecule by identifying the magnifying tags associated with the target nucleic acid molecule.

Cont
Cl 9

Claim 43. The method as claimed in Claim 42, wherein 2 or more bases are sequenced per cycle.

Claim 44. The method as claimed in Claim 43, wherein 4 or more bases are sequenced per cycle.

Claim 45. The method as claimed in Claim 42, wherein the signal associated with each base is magnified by increasing the number of times that said base appears in said sequence.

Claim 46. The method as claimed in Claim 42, wherein the resulting magnified signal is converted into readable signals and said sequencing is carried out by assessing the readable signals.

Claim 47. The method as claimed in Claim 46, wherein each readable signal comprises a pattern made up of a single signal event which creates a unique signal on each magnifying tag.

Claim 48. A method of sequencing all or part of a target nucleic acid molecule comprising the steps of:

(A) determining the sequence of a portion of said target nucleic acid molecule;

(B) determining the position of said portion within said target nucleic acid molecule; and

(C) combining the information obtained in steps (A) and (B) to obtain the sequence of all or part of said target nucleic acid molecule.

Claim 49. The method as claimed in Claim 48, wherein said position is determined by reference to a positional marker.

Claim 50. The method as claimed in Claim 48, wherein said position is determined by reference to a restriction map of said target nucleic acid molecule.

Claim 51. The method as claimed in Claim 48, wherein the portion which is sequenced has 4 or more bases and/or the position of said portion within said target nucleic acid molecule is determined with an accuracy of less than 1 kb.

Claim 52. The method as claimed in Claim 48, wherein said portion is sequenced by identifying magnifying tags associated with the target nucleic acid molecule, wherein said magnifying tags correspond to one or more bases of an adapter binding region or to one or more bases in proximity to an adapter binding region, wherein said adapter binding region binds an adapter molecule which comprises:

(i) one or more of said magnifying tags, or

(ii) a means for attaching one or more of said magnifying tags.

Claim 53. The method as claimed in Claim 48, wherein the sequence of the target nucleic acid molecule is determined by assessing the complementarity of a portion of said target nucleic acid molecule by a process comprising the steps of:

(i) treating said target nucleic acid molecule so that at least a region of said target nucleic acid molecule is converted into a form suitable for binding a complementary probe, wherein said complementary probe is bound to a solid support or said complementary probe carries a means for attaching to a solid support;

(ii) binding said complementary probe to at least a portion of said region suitable for binding a complementary probe;

(iii) optionally repeating steps (i) and (ii), with the *proviso* that said complementary probe binds to an adjacent or overlapping region of said target nucleic acid molecule relative to the region to which the complementary probe of the previous cycle bound; and

(iv) determining the sequence of said target nucleic acid molecule by identifying the complementary probe(s) to which said target nucleic acid molecule bound.

Claim 54. The method as claimed in Claim 53, wherein in step (i) said form is a single-stranded nucleic acid molecule.

Claim 55. The method as claimed in Claim 53, wherein in step (ii) said portion is 4 to 12 bases in length.

Claim 56. The method of as claimed in Claim 43, wherein a portion of said sequence is determined by identifying magnifying tags associated with the target nucleic acid molecule, wherein said magnifying tags correspond to one or more bases of an adapter binding region or to one or more bases in proximity to an adapter binding region, wherein said adapter binding region binds an adapter molecule which comprises:

(i) one or more of said magnifying tags, or

(ii) a means for attaching one or more of said magnifying tags; and

an adjacent or overlapping portion of said sequence is determined by a process comprising the steps of:

(i) treating said target nucleic acid molecule so that a region of said target nucleic acid

Cont A19

molecule is converted into a form suitable for binding a complementary probe, wherein said complementary probe is bound to a solid support or said complementary probe carries a means for attaching to a solid support;

(ii) binding said complementary probe to at least a portion of said region suitable for binding a complementary probe;

(iii) optionally repeating steps (i) and (ii), with the *proviso* that said complementary probe binds to an adjacent or overlapping region of said target nucleic acid molecule relative to the region to which the complementary probe of the previous cycle bound; and

(iv) determining the sequence of said target nucleic acid molecule by identifying the complementary probe(s) to which said target nucleic acid molecule bound.

Claim 57. A kit for magnifying one or more bases of a target nucleic acid molecule comprising at least one or more adapter molecules as defined in Claim 26.

Claim 58. The kit as claimed in Claim 57, wherein said adapter molecules are attached to one or more solid supports.

Claim 59. The method as claimed in Claim 26, wherein said method is performed on a sample comprising a heterogeneous mixture of target nucleic acid molecules.

Claim 60. The method as claimed in Claim 42, wherein said method is performed on a sample comprising a heterogeneous mixture of target nucleic acid molecules.

Claim 61. The method as claimed in Claim 48, wherein said method is performed on a sample comprising a heterogeneous mixture of target nucleic acid molecules.

Claim 62. A method of producing a map of a target nucleic acid molecule comprising the steps of:

(A) obtaining sequence information on portions of a target nucleic acid molecule by cleaving said target nucleic acid molecule with one or more nucleases; and

(B) binding an adapter molecule to a region of said target nucleic acid molecule, wherein said adapter molecule comprises one or more magnifying tags as claimed in Claim 26,

wherein each tag comprises:

(i) a first signaling moiety which corresponds to one or more bases of said region to which said adapter molecule binds, and

(ii) a second signaling moiety which corresponds to a nuclease used for cleavage,

wherein said portions comprise all or part of the cleavage sites of said nucleases and/or all or part of the restriction sites of said nucleases; and

(C) determining the position of said portions within said target nucleic acid molecule so to produce a map of the target nucleic acid molecule.

Claim 63. The method as claimed in Claim 62, wherein said nuclease has a cleavage site which is separate from its recognition site.

Claim 64. The method as claimed in Claim 62, wherein said cleaving produces complementary single-stranded regions. --

IN THE ABSTRACT:

Please insert the Abstract attached hereto.

SEQUENCE LISTING:

Please insert the Sequence Listing filed simultaneously herewith.

REMARKS

The specification has been amended to insert formal matter; Claim 1-25 have been cancelled and new Claims 26-60 are being amended in order to remove improper dependency and conform with U.S. patent practice; and the Abstract and Sequence Listing has been added in order to make the application consistent with U.S. patent practice.

The Examiner is requested to note that Applicant simultaneously files herewith a Sequence Listing (which is considered to be a separate document by the U.S. Patent and Trademark Office) in PatentIn Version 3.0.